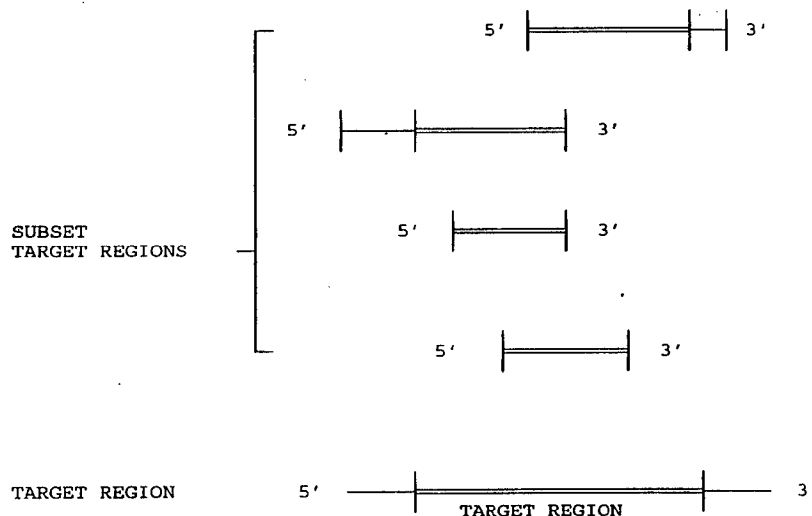




INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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(74) Agents: HEBER, Sheldon, O. et al.; Lyon & Lyon, First Interstate World Center, Suite 4700, 633 West Fifth Street, Los Angeles, CA 90071-2066 (US).			

(54) Title: ENHANCEMENT OF OLIGONUCLEOTIDE INHIBITION OF PROTEIN PRODUCTION, CELL PROLIFERATION, AND/OR MULTIPLICATION OF INFECTIOUS DISEASE PATHOGENS



(57) Abstract

The invention features the use of a purified first targeted oligonucleotide in combination with either 1) a subtargeted oligonucleotide, 2) second targeted oligonucleotide, or 3) a non-targeted phosphorothioate oligonucleotide, to inhibit protein production of a targeted nucleic acid sequence, cell proliferation, and/or the multiplication of a foreign organism. The subtargeted oligonucleotide contains a truncated version of the targeted oligonucleotide.

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## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 94/08334

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 6 C12N15/11 C12N9/00 A61K31/70 A61K48/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C12N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO,A,93 15194 (WORCESTER FOUNDATION FOR EXPERIMENTAL BIOLOGY) 5 August 1993  *see the whole patent* ----	6-11, 29-35, 50,53, 61,62
P,X	NUCLEIC ACIDS RESEARCH, vol. 21, no. 17, 1993 pages 4119-4125, R.B. DENMAN 'Cleavage of full length APP mRNA by mannerhead ribozymes' *see the whole article* ----- -/--	6-8,29, 31

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

18 July 1995

Date of mailing of the international search report

14.08.95

Name and mailing address of the ISA

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Marie, A

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 94/08334

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP,A,0 318 245 (M-L. TECHNOLOGY VENTURES, L.P.) 31 May 1989	7,29,31,50
Y	*see the whole patent*	8-11,19-23,30,32-35,44-49,52,53,61,62
X	NUCLEIC ACIDS RESEARCH, vol. 16, no. 8, 1988 pages 3341-3358, L.J. MAHER III ET AL. 'Comparative hybrid arrest by tandem antisense oligodeoxyribonucleotides or oligodeoxyribonucleotide methylphosphonates in a cell-free system'	6-8,29,31,50
Y	*see the whole article*	
Y	*see the whole article*	8-11,30,32-35,52,61,62
X	NUCLEIC ACIDS RESEARCH, vol. 20, no. 17, 1992 pages 4607-4612, J. GOODCHILD 'Enhancement of ribozyme catalytic activity by a contiguous oligodeoxynucleotide (facilitator) and by 2'-O-methylation'	6-9,29,31,33,50,53
Y	*see the whole article*	
Y	*see the whole article*	10,11,30,32,34,35,61,62
Y	EP,A,0 288 163 (THE UNITED STATES OF AMERICA) 26 October 1988	19-23,44-49,53
	*see the whole patent*	
Y	FASEB JOURNAL, vol. 7, no. 1, 1993 pages 106-112, J.M. BURKE ET AL. 'In vitro selection and evolution of RNA...'	42,43
	*see the whole article*	
Y	WO,A,92 14843 (GILEAD SCIENCES, INC.) 3 September 1992	42,43
	*see the whole patent*	

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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 94/08334

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>BIOCHEMISTRY, vol. 28, 1989 pages 1340-1346, C. MAJUMDAR ET AL. 'Stepwise mechanism of HIV reverse transcriptase: primer function of phosphorothioate oligodeoxynucleotide' *see the whole article*</p> <p>-----</p>	<p>19-23, 44, 53</p>

**Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

1. Claims: 1-5, 12-18, 24-28, 36-41, 51, 53 (partially); 54-60 (complete)
2. Claims: 6-11, 29-35, 50, 53 (partially); 61, 62 (complete)
3. Claims: 19-23, 44-49, 52, 53 (partially)
4. Claims: 42, 43

1. ☒ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 94/08334

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO-A-9315194	05-08-93	AU-B-	3597793	01-09-93
		CA-A-	2117428	05-08-93
		EP-A-	0625194	23-11-94
-----				
EP-A-0318245	31-05-89	US-A-	5030557	09-07-91
		AT-T-	106947	15-06-94
		AU-A-	2611288	14-06-89
		CA-A-	1319336	22-06-93
		DE-D-	3850055	14-07-94
		DE-T-	3850055	29-09-94
		ES-T-	2056115	01-10-94
		JP-T-	2502250	26-07-90
		WO-A-	8904876	01-06-89
-----				
EP-A-0288163	26-10-88	US-A-	5276019	04-01-94
		AT-T-	116857	15-01-95
		AU-B-	619180	23-01-92
		AU-A-	1571788	02-11-88
		DE-D-	3852714	23-02-95
		DE-T-	3852714	24-05-95
		JP-T-	1503302	09-11-89
		WO-A-	8807544	06-10-88
		US-A-	5264423	23-11-93
US-A-	5286717	15-02-94		
-----				
WO-A-9214843	03-09-92	AU-A-	1435492	15-09-92
		EP-A-	0572529	08-12-93
		JP-T-	6508022	14-09-94
		AU-A-	1456092	15-09-92
		WO-A-	9214842	03-09-92
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